TECHNICAL SUPPORT FOR HUMAN HEALTH RISK ASSESSMENT AND RELATED ACTIVITIES
EP-C-17-015,
Task Order No. TBD
PERFORMANCE WORK STATEMENT (PWS)
PR-ORD-18-02692

September 24, 2018; modified February 5, 2019

TITLE: Advancing Pb Exposure and Biokinetic Modeling for EPA Regulatory Decisions and Site Assessments

PERIOD OF PERFORMANCE: Two years from approval of task order award.

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I. PURPOSE

The purpose of this task order is to provide services to assist the U.S. Environmental Protection Agency's (EPA) National Center for Environmental Assessment (NCEA), Office of Research and Development (ORD), in the development and evaluation of computational models to estimate the disposition of lead (Pb) in humans in support of the EPA's Superfund Program and other program offices relying on biokinetic models for Pb.

II. BACKGROUND

The Integrated Exposure Uptake Biokinetic (IEUBK) Model for Pb in Children (v. 0.99d) was released in 1994 and has been widely accepted in the risk assessment community as a tool for site-specific risk assessments related to childhood Pb exposure. The IEUBK model was designed to assess changes in blood Pb of children under seven years of age over periods of a month or more. Prior evaluations of the IEUBK model were completed using datasets where children's blood Pb levels (BLL) exceeded those currently observed in NHANES surveys. A new version of the IEUBK model (v. 2.0) has been developed and contains default values (e.g., soil/dust ingestion rates) different from those used during prior model evaluations. Decreasing childhood BLL in the U.S. and a change in influential default values in the IEUBK model (v. 2.0) both mandate an evaluation the predictive ability of the model prior to public release.

Recognizing the need to model changes in BLL for intermittent Pb exposures in both children and adults, EPA's Office of Research and Development (ORD), in collaboration with Office of Chemical Safety and Pollution Prevention (OCSPP), developed an All-Ages Lead Model (AALM). The AALM provides a tool for rapidly evaluating the impact of possible sources of Pb on Pb concentrations in blood and other tissues of humans from birth to 90 years of age. The AALM will allow users to assess the effects of both intermittent Pb exposures and stable exposure conditions. Implemented in Fortran with an Excel user interface, the current version of the model should be readily usable. Efforts are underway to have the AALM reviewed by EPA's Science Advisory Board (SAB).

III. STATEMENT OF WORK

Objective

The objective of this task order is to assist NCEA in evaluating the predictive ability of the IEUBK model (v. 2.0) and to continue development of the AALM. The evaluation of the IEUBK model will require observed children's BLL paired with environmental media concentrations necessary to predict BLL in the IEUBK model. The continued development of the AALM will consist of expanding model capabilities including stochastic exposure scenarios, performing limited model evaluations, preparing for and attending SAB peer-review meeting, and assisting with responses to peer-review comments. Specific tasks are described below.

Task 1: Technical Cost Proposal and Staffing Plan

The contractor shall prepare a Technical Proposal describing how the work outlined in this Task Order PWS will be performed, including deliverables, a schedule, estimated labor hours, and cost proposal. The contractor shall also prepare a Staffing Plan that shows assigned personnel by task. Both the Technical Cost Proposal and Staffing Plan

shall be submitted within (10) calendar days of receipt of the Performance Work statement (PWS).
The contractor shall provide highly qualified personnel to perform services required under this Task Order. The senior contributors shall have earned a terminal degree in their field of expertise (e.g., PhD, ScD, MD, and DVM). Previous experience in searching for and identifying studies, reports, and other data streams relevant to informing hazard and dose-response evaluation of chemicals for the EPA is also required.
Delivery Schedule: Due 10 calendar days after receipt of the PWS.

Task 2: Kick-Off Conference Call
Within two (2) workdays after receipt of approved Task Order, the contractor shall schedule a conference call with the EPA TOCOR to discuss all tasks and to clarify any specific issues. The contractor shall distribute meeting minutes of the topics discussed and any action items agreed to within three (3) workdays after the conference call.

Delivery Schedule: Conference call scheduled within 2 workdays after receipt of approved Task Order and distribution of meeting minutes within 3 workdays after the conference call.

Task 3: Develop a Project-Specific Quality Assurance Project Plan (QAPP);
The contractor shall submit a Project-Specific Quality Assurance Project Plan (QAPP) that addresses data collection, model evaluations, and model refinements. The QAPP should include a description of quality control checks to verify accuracy, completeness, and adherence to established format. The contractor shall address in the QAPP how existing data will be considered for the Task Order. The EPA General Assessment Factors Handbook provides guidance for evaluating existing data and information, (https://www.epa.gov/risk/summary-general-assessment-factors-evaluating-quality-scientific-and-technical-information). Existing (secondary) data are defined data that were developed for a different purpose and include data in the published literature. The QAPP shall conform with EPA's Requirements for Quality Assurance Project Plans (EPA QA/R-5). Guidance for developing QAPPs that meet EPA specifications prepared for activities conducted by or funded by EPA, are available online at http://www.epa.gov/quality/qa_docs.html, see "EPA Requirements for Quality Assurance Project Plans (QA/R-5)". The EPA QAPP ID: B-RTP-0031816-QP-1-0 shall be displayed on the QAPP cover page.

Please note that the QAPP needs to describe the use of data acquired at the Bunker Hill Superfund site, QA related to the model evaluation, and model development, i.e., all QA aspects related to the full scope of tasks described in this PWS. EPA NCEA's Quality Assurance manager must approve the QAPP (existing or modified) before work on this order begins. The contractor shall coordinate a meeting of the project team after completion of the QAPP and Work Plan prior to the beginning of the data analysis.

Strict adherence to confidentiality and protection of personal identifiable information shall be maintained by anyone with access to the data in accordance with EPA Policy 2151.0: Privacy Policy https://www.epa.gov/privacy/epa-policy-21510-privacy-policy.

Delivery Schedule: Due 5 working days after award of Task Order.

Task 4 – Obtain access to blood Pb and environmental data necessary for IEUBK model evaluation, develop data files necessary for proposed analyses, and perform evaluation.

Task 4a – EPA proposes to use data acquired at the Bunker Hill Superfund Site in Idaho for evaluation of the IEUBK model (v. 2.0). The evaluation of the IEUBK model will require children's BLL paired with environmental media concentrations necessary to predict BLL in the IEUBK model. Ideally, data should uniformly span all age ranges in the IEUBK model. The IEUBK model requires inputs of environmental concentrations of Pb in air, water, soil, and indoor dust as well as soil and dust bioavailability. The contractor shall establish a cohort of children with BLL measurements linked with residential addresses for model evaluation using Pb concentrations in relevant environment media (soil, dust, water and air) over time and bioavailability for soil and dust. It is preferable that data from 2000 to the present be utilized such that the revised IEUBK (v. 2.0) model can be evaluated at lower average BLL than previously done by Hogan et al. (Environ Health Perspect., 106(S6):1557-1567, 1998) where geometric BLL of children were in excess of 5 µg/dL.

After linking BLL with environmental media data, the contractor shall provide a brief report summarizing the available data proposed for the model evaluation. The report should provide children's ages, sex, BLL, and environmental media Pb concentrations grouped by year and basic geographical location (e.g., community level). If survey data are available and the children are known to be at multiple locations where they may be potentially exposed to Pb, it may be necessary to time-weight the media concentrations. Other summary data (e.g., the dates/season of blood samples and whether venous or capillary samples) should be provided as the contractor deems necessary to assess the utility of the data for the IEUBK evaluation. The contractor shall also outline the approach for conducting the IEUBK model evaluation within the draft report. To the extent possible, it is expected that the contractor should use approaches similar to Hogan et al. (1998) where comparisons of predicted and observed BLL were made between communities and at the individual level.

Delivery Schedule: Draft report describing data to be used and approach for model evaluation due 30 calendar days after the QAAP has been signed by all parties. EPA will review within 7 days and may request clarification or revision to be completed by the contractor within 7 days.

Task 4b – The contractor shall use the dataset and evaluation approaches developed under Task 4a to evaluate the IEUBK model's predictive ability. Batch files for IEUBK should be developed for the comparisons between observed and predicted BLL. It is understood by EPA that individual level data linking children's BLL and media concentrations in the batch files cannot be released to EPA for privacy concerns. Any other site-specific data (e.g., soil bioavailability) appropriate for the model evaluation should be used for the evaluation. Where site-specific data are not available, default model values should be used. Should additional datasets become available to the contractor or EPA, specific technical direction will be provided by the TOCOR related to their potential use in model evaluations.

It is expected that an evaluation should be completed using at least three separate soil/dust

ingestion rates: (1) the IEUBK (v. 2.0) default from von Lindern et al. (2016), (2) the EPA Exposure Factor Handbook (2017), and (3) the IEUBK (v. 1.1 Build 11) defaults. In consult with EPA, the contractor may use other input data for the evaluation.

Another aspect that may need evaluation is elimination rates in the IEUBK model. To match predicted and observed blood lead levels using the current default ingestion rates in IEUBK (v. 1.1, Build 11), elimination rates were set to the high end of the biologically plausible range. Use of lower ingestion rates than in IEUBK (v. 1.1, Build 11) may decrease in slope factor between soil Pb concentration and blood Pb. However, lowering elimination rates would increase the slope factor between Pb uptake and blood Pb (i.e., a greater increase in blood Pb per µg/day of Pb uptake). A change in the slope factor between Pb uptake and blood Pb would change the alignment of the IEUBK model with baboon data (Harley and Kneip, 1985) and nullify the results of the von Lindern et al. (2016) study. For these reasons, the relationships between lower ingestion rates and lead output (urinary and excretion) must be carefully considered to determine if a lower ingestion rate would impact the model's predictive ability.

The contractor shall prepare a draft report describing the results of IEUBK model evaluation. This draft report should be an extension of the report completed under Task 4a. The report should document other site-specific sources of Pb exposure, such as Pb-based paint, age of the housing stock, and food. The report should include discussion of the ability to account for these sources in the model evaluation. Where available, behavioral and demographic data for children such at time spent outside or away from home should be provided in the report and recognized as a source of uncertainty. The report should include summary tables and figures describing site-specific trends in BLL data over the period that the data span. Summary tables and figures should illustrate the predictive ability of the IEUBK model.

Delivery Schedule: Draft report describing data to be used, approaches, and results of the IEUBK model evaluation are due 60 calendar days after EPA acceptance of Task 4a report. Due to potential interest in this draft report by Superfund and Regional Offices, EPA may require one or more teleconference calls between the contractor, TOCOR, the EPA Technical Review Workgroup for Pb, and/or other EPA management and staff. EPA anticipates providing comments on the draft evaluation report within 30 days of delivery. Depending on the nature and extent of comments on the report, the contractor is expected to perform additional analyses and revise the report within 30 days following receipt of comments from EPA.

Task 4c – Following acceptance of the Task 4b deliverable, the contractor shall prepare a manuscript describing the IEUBK model evaluation that conforms to the submission guidelines of Environment Health Perspectives or another journal agreed upon between the contractor and the TOCOR. Teleconferences between the TOCOR and contractor may be required to efficiently address comments received on the draft manuscript at multiple stages of this subtask.

Delivery Schedule: A draft manuscript will be due to EPA 30 days after initiating this subtask.

The draft manuscript will be submitted by the TOCOR for an internal EPA technical manuscript review. The contractor may, at their discretion, suggest one or more potential EPA reviewers and one reviewer external EPA. Depending on the nature and extent of comments on the

manuscript, the contractor is expected to revise the manuscript within 30 days following receipt of comments from EPA. The revised manuscript will be submitted by the TOCOR for EPA manuscript clearance, a process that my take 60 or more days to complete. The contractor shall revise the manuscript within 30 days (depending on the nature of comments) following receipt of manuscript comments from EPA.

Following ORD clearance of the manuscript for publication, the contractor shall submit the manuscript to the chosen journal. The contractor shall revise the manuscript within 30 days (depending on the nature of comments) following receipt of manuscript comments from the journal peer-reviewers.

Task 5 – Continue development and evaluation of the AALM.

Task 5a – The contractor shall develop a user-friendly interface for batch runs of the AALM. The batch run module should not require the users to purchase software packages beyond Microsoft Excel which is used for the AALM user interface. The interface should support model evaluations of the AALM such as those described above under Task 4b for the IEUBK model. The batch run module for the AALM should have the flexibility to handle most of the complex exposure scenarios possible in the AALM, but will not be required to output data beyond that required for performance of Task 5c. In designing the batch run module, consideration should be given to the development of a module that can been further extended for performance as described under Tasks 6a and 6b. The contractor shall also prepare a brief set of instructions describing how to use the batch run module. These instructions should pertain to the batch run module itself and are not expected to cover other technical or scientific aspects of the AALM.

~~**Task 5b** – EPA proposes to use data acquired at the Bunker Hill Superfund Site in Idaho for evaluation of the AALM. The contractor shall establish a cohort of adolescents (ages 7-17 years) and adults with BLL measurements linked with residential addresses for model evaluation using Pb concentrations in relevant environment media (soil, dust, water and air).~~

~~After linking BLL with environmental media data, the contractor shall provide a brief report summarizing the available adolescents and adult data and proposed approaches for the model evaluation. The report should provide ages, sex, BLL, and environmental media Pb concentrations grouped by year and/or basic geographical location (e.g., community level). If available, the report should document other sources of Pb exposure, such as schools or occupation, Pb-based paint, and housing. The report should include details related to the ability to account for these or other sources in the model evaluation. If adults are known to be exposed to Pb at multiple locations and concentrations, it may be necessary to record and account for the location-specific fraction of Pb exposure in a media.~~

~~**Task 5c** – Evaluate the AALM using children and adult data compiled under Tasks 4a and 5b, respectively. Batch files for AALM should be developed for the comparisons between observed and predicted BLL. Any other site-specific data (e.g., soil bioavailability) appropriate for the model evaluation should be entered into the AALM for the evaluation. Where site-specific data are not available, default model values should be used. Should additional datasets become~~

~~available to the contractor or EPA, specific technical direction will be provided by the TOCOR related to their potential use in model evaluations.~~

~~The contractor shall prepare a draft report describing the results of the AALM model evaluation. This draft report should be an extension of the reports completed under Task 4a and 5b. The report should document other site-specific sources of Pb exposure, such as Pb-based paint, age of the housing stock, and food. The report should include discussion related to the ability to account for these sources in the model evaluation. Where available, behavioral and demographic data for the children and adults such at time spent outside or away from home at childcare facilities, schools, or place of employment should be provided in the report and/or recognized as a source of uncertainty. The report should include summary tables and figures describing site-specific trends in BLL data over the period from which data spanned. Summary tables and figures should illustrate the predictive ability of the AALM model.~~

Task 6 – Extend capabilities of the AALM to perform stochastic analyses.

Task 6a – Adapt the batch run module for the AALM developed under Task 5a for more diverse outputs. The contractor shall modify the batch run module for the AALM to offer (1) the potential to output Pb concentrations in multiple body compartments, e.g., blood and bone; (2) at several discrete ages specified by the user, and (3) as an average Pb concentration in compartments over some age period, e.g., from age 1 to the 6th birthday. The batch run module should not require the users to purchase software packages beyond Microsoft Excel which is used for the AALM user interface. The contractor shall also prepare a brief set of instructions describing how to use the batch run module. These instructions should pertain to the batch run module itself and are not expected to cover other technical or scientific aspects of the AALM.

Task 6b – In Zartarian et al. (2017; https://doi.org/10.1289/EHP1605), EPA provided the results of analyses obtained from the IEUBK model linked to the Stochastic Human Exposure and Dose Simulation (SHEDS)–Multimedia Model. Under this task, EPA seeks to extend this functionality to the AALM, i.e., SHEDS linked with the AALM.

Adapt the batch run module developed under Task 6a to accept input media concentrations directly from SHEDS-multimedia. The contractor shall extend the batch run capabilities to simulate distributional inputs and distribution outputs that may be accessed for additional statistical analyses. As SHEDS-multimedia requires users have SAS 9.1 or higher installed, it is anticipated and acceptable for contractor to use SAS functionality in the performance of this subtask. The contractor shall also prepare a brief set of instructions describing how to use the batch run module linking SHEDS and the AALM. These instructions should pertain to use of the linked SHEDS-AALM module itself and are not expected to cover other technical or scientific aspects of the AALM or SHEDS.

~~**Task 6c** – The contractor shall evaluate the predictive ability of SHEDS-AALM (EPA will provide code developed for the Zartarian et al. 2017 publication) and possibly SHEDS-AALM with local scale data. Pending successful evaluations of the IEUBK model under Task 4, the contractor shall attempt a local scale evaluation of SHEDS-IEUBK using the Bunker Hill site data. Pending successful evaluations of the AALM model under Task 5, the contractor shall~~

~~attempt a local scale evaluation of SHEDS-AALM using the Bunker Hill site data. Other specific analyses are to be determined. Should additional datasets become available to the contractor or EPA, specific technical direction will be provided by the TOCOR related to their potential use in model evaluations.~~

Task 7 – Assist with preparation for and response to SAB peer-review of AALM.

Task 7a – Efforts are underway to have the AALM peer-reviewed by the SAB. The contractor shall assist EPA with preparation and/or review of briefing materials and other documents (if necessary) for the in-person SAB peer-review meeting of the AALM.

Task 7b –The contractor shall attend and participate in the SAB peer-review meeting of the AALM. The two-day meeting is expected to take place in Washington, DC.

~~**Task 7c** – The contractor shall revise his/her written sections, the AALM model software (i.e., executable) and user interface based on recommendations resulting SAB meeting. Response to comments shall be delivered to the TOCOR within 2 months after receiving the written comments from SAB.~~

Deliverables Table

Deliverables	Time
Task 1. Cost Proposal and Staffing Plan	10 days after receiving PWS
Task 2. Schedule Kick-off call	2 workdays after award of task order
Task 2. Kick-off call minutes	3 workdays after call
Task 3. QAPP	5 workdays after award of task order
Task 4a. Draft report summarizing data available for IEUBK evaluation	30 calendar days after QAPP signed
Task 4b. Draft report summarizing evaluation of IEUBK	60 calendar days after Task 4a report is accepted by EPA
Task 4c. Draft manuscript Submit manuscript for publication	30 calendar days after Task 4b report is accepted by EPA 30 calendar days after ORD clearance
Task 5a. Batch run interface for AALM and provide written operating instructions	6 months after award of task order
~~Task 5b. Draft report summarizing data available for AALM evaluation~~	~~7 months after award of task order~~
~~Task 5c. Draft report summarizing evaluation of AALM~~	~~9 months after award of task order~~

Task 6a. Adapt batch run module for more diverse output capabilities for AALM and provide written operating instructions	To be determined, may be conducted in parallel with Task 5
Task 6b. Adapt batch run module for AALM to accept SHEDS input, output distributional results, and provide written operating instructions	To be determined, may be conducted in parallel with Task 5
~~Task 6c. Perform SHEDS-IEUBK and SHEDS-AALM evaluations~~	~~To be determined, may be conducted in parallel with Task 5~~
Task 7. Assist with preparation for and response to SAB peer-review of AALM	SAB currently preparing for review, schedule is not yet known

IV. SPECIAL CONDITIONS AND MANAGEMENT CONTROLS

Project Meetings

Project meetings between the contractor and TOCOR shall be conducted as needed, but not less than every two months, to assure the completion of the PWS. The contractor and/or the TOCOR may request a conference call via email during the performance of or of completion of any tasks for technical direction, clarification, status updates, or other needs. The contractor shall provide, at a minimum, the following up-to-date information at each meeting:

- Status and progress of tasks
- Preliminary findings from the data analysis
- Problems encountered and resolutions
- Requests for technical direction
- Logistic concerns

The need for face-to-face meetings and travel is not anticipated other than for the completion of Task 7 in relation to a public meeting for a SAB review of the AALM.

Monthly Reports

Monthly reports summarizing the status of the PWS shall be completed and emailed to the TOCOR, Alt-TOCOR, and COR. Monthly reports should include:

- Planned activities for the upcoming period
- Status and progress of tasks
- Problems encountered and resolutions
- Hours expended sorted by level
- Financial Status

Technical Expert Qualifications

1. The contractor shall certify there is no conflict of interest. The contractor shall provide the following conflict of interest certification in the Technical Proposal:

I certify that, to the best of my knowledge and belief, no actual, apparent, or potential organizational or individual conflicts of interest related to this task order exist. Personnel who perform work under this task order, or relating to the task order, have been informed of their obligation to report personal and organizational interest. All actual, apparent or potential organizational or individual conflicts of interest related to this task order have been reported to the Contracting Officer and Contract-level COR.

2. The contractor shall be responsible for obtaining a conflict of interest certification for any subcontractor services.

3. All deliverables will be reviewed for conformance to the requirements of this Task Order before being approved as final.

4. The contractor shall comply with other applicable requirements for final task order reports stipulated in the contract.

Notice Regarding Guidance Provided Under This Project

Guidance is strictly limited to technical and analytical support. The contractor shall not engage in activities of an inherent governmental nature such as the following:

(1) Formulation of Agency policy
(2) Selection of Agency priorities
(3) Development of Agency regulations

Should the contractor receive any instruction from an EPA staff person that the contractor ascertains to fall into any of these categories or goes beyond the scope of the contract or task order, the Contractor shall immediately contact the COR and TOCOR.

Performance Standards and Quality Measures

Tasks are to be evaluated in accordance with the Quality Assurance Surveillance Plan and Quality Management Plan identified in the contract.